UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/828,474	04/20/2004	Tianmin Zhu	AM101007	7099

25291 7590 12/11/2007

WYETH
PATENT LAW GROUP
5 GIRALDA FARMS
MADISON, NJ 07940

EXAMINER	
FARZANEH, SHAHRZAD	
ART UNIT	PAPER NUMBER
4173	

MAIL DATE	DELIVERY MODE
12/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/828,474	ZHU ET AL.	
	Examiner	Art Unit	
	SHAHRZAD FARZANEH	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-96* is/are pending in the application.

4a) Of the above claim(s) *9-67 and 74-96* is/are withdrawn from consideration.

5)☒ Claim(s) *68-73* is/are allowed.

6)☐ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on 9/19/2007 is acknowledged. The traversal is on the ground(s) that all groups can be searched without serious burden and that the claims all classified in the same class and subclass. This is not found persuasive because in the instant case, the inventions of Groups II and III, the process of making the drug conjugate polymer of claim 68 (Formula III) and 74 (Formula IV) of the invention claimed in Group I, step c) discloses adding mPEG-sulfhydryl 5000 to the solution of step b). Since the compound itself is claimed to have 1-1000 units for the n group, and mPEG-sulflhydryl 5000 indicates a chain of 5000 units, the process can be used to make another materially different product. Furthermore, the method as claimed in the invention of Group III discloses adding an amine to the compound of claim 50, in the invention of Group I. The amine group differs significantly in scope from an ethyl group, hence this method can be use to make a materially different product. The inventions claimed in Groups I, II and III are all patentably distinct inventions.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 9-67 and 74-96 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9/12/2007.

Specification

1. The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. The specification is objected to because essential material for describing wortmannin derivatives other than Formulas I, II, III, IV and V due to improper incorporation by reference to printed non-patent publications. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-8 are rejected less than 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Essential material for describing wortmannin derivatives other than Formulas

I, II, III, IV and V is to improper incorporation by reference to printed non-patent publications. Thus, an ordinarily skilled artisan would be unable to envisage the claimed invention.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by L.Varticovski et al. (Journal of Controlled Release Volume 74, Issues 1-3, 6 July 2001, Pages 275-81).

The above reference discloses with regard to instant claims 1-6 activation of phosphoinositide 3-kinase (PI 3-kinase) is essential for signal transduction by many growth factors and oncogenes and may contribute to tumor progression (see abstract, line 2-3). The reference goes on to teach wortmannin, a fungal metabolite, which is a potent inhibitor of PI 3-kinase; wortmannin covalently modifies the PI 3-kinase catalytic subunit. Because wortmannin is soluble only in organic solvents and unstable in water, there are difficulties in its use in vivo. To generate a water-soluble wortmannin derivative, a conjugate of HPMA copolymer and DAWM (a substituted wortmannin derivative) is prepared. The attachment of DAWM to HPMA copolymer containing oligopeptide side chains was covalently attached (see abstract lines 4-9). The final product had a molecular mass of 20kDa and contained 2 wt % of DAWM (see abstract line 10).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 3-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Varticovski et al. as applied to claims 1 and 2 above, and in view of Cardenas et al. and Razzini et al.

7. Varticovski et al. teaches a HPMA copolymer covalently attached to a wortmannin derivative as a water-soluble derivative that is active in both in vivo and in vitro and blocks PI 3-kinase activity. Varticovski et al. further teaches the new HPMA copolymer wortmannin derivative conjugate can be further modified to allow cell specific targeting and may be useful in investigations of the role of PI 3-kinase in angiogenesis, tumor progression, and specific intracellular functions in vivo (see conclusion, line 4-6, see Material and Methods section 2.3

and Results section 3.2). Varticovski does not teach; however, the inhibition of mTOR-kinase-kinase inhibition.

8. Cardenas et al. teaches that wortmannin is an art recognized inhibitor of both PI 3-kinase and mTOR-kinase-kinase. PI 3-kinase and mTOR-kinase-kinase are in the same family of enzymes (see section 3.0, page 7, and table 1.0, page 15). The structurally distinct PI 3-kinase inhibitor has been used to confirm the effects of wortmannin attributed to inhibition of PI 3-kinase, but this compound also inhibits mTOR-kinase and may inhibit other wortmannin targets as well. Hence more enzyme-specific analogues of wortmannin would be valuable reagents to probe the intracellular functions of this family of enzymes (see page 8, first paragraph, lines 2-5). Cardenas et al further teaches the potential of signaling cascades in oncology and infectious disease (see conclusion page 14, last sentence).

9. Varticovski et al. and Cardenas et al. do not teach; however, that PI 3-kinase inhibition is known to have therapeutic effects on several types of cancer, of which non-small-cell lung cancer is a part. This deficiency is overcome by the range of mammalian cancers that PI 3-kinase inhibition is effective.

10. The teaching of Razzini et al. teaches new efforts in cancer therapy, focused on signaling pathways show that PI 3-kinase potentially being necessary for a range of cancer-related functions (see abstract, line 1-3). Examples of cancers taught in Razzini et al. are human breast cancer, small-cell lung cancer, and ovarian cancer. Hence, one ordinarily skilled in the art would have a reasonable expectation that PI 3-kinase inhibition results in effective treatment of cancer, and as such would be motivated to try administering PI 3-kinase in the method of treatment of non-small cell lung cancer.

11. Thus, Razzini et al. motivates or suggests combining of its teachings along with the teachings of Varticovski et al. and Cardenas et al. to result in the claimed invention of the dependent instant claims 7 and 8. Razzini et al. is suggestive of the method of treating cancer with the inhibition of PI 3-kinase in a variety of cancers.

12. Furthermore, the in vitro data of mammalian cell line inhibition of PI 3-kinase, as taught in Varticovski, et al. suggests reasonably successful PI 3-kinase inhibition in vivo.

13. It would have been prima facie obvious to one skilled in the art at the time of the invention to covalently attach a water-soluble polymer to wortmannin derivative to inhibit PI 3-kinase, mTOR-kinase, and; hence treat various types of cancer, including non-small cell lung cancer. As evidenced by the teaching of Varticovski et al., HPMA copolymer covalently attached to a wortmannin derivative, the water-solubility of wortmannin is improved and can be used as an inhibitor of PI 3-kinase and tumor progression, as would therefore be encompassed the sub-species of non-small cell lung cancer. As evidenced by the teaching of Cardenas et al., wortmannin is a known antiproliferative as well as mTOR-kinase-kinase, which is in the same family of enzymes as PI 3-kinase, and; hence, would be an antiproliferative for the inhibition of both enzymes. An ordinarily skilled practitioner would have been motivated to administer the HPMA copolymer covalently attached to wortmannin derivative, as taught by Varticovski, et al. to treat non-small cell lung cancer, as it is a disease that which inhibition of PI 3-kinase and mTOR-kinase-kinase is reasonably expected results in effective in the treatment of such cancer.

Allowable Subject Matter

14. Claims 68-73 are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHAHRZAD FARZANEH whose telephone number is (571)270-1557. The examiner can normally be reached on Weekly 7:30-5:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SF

/Ardin H Marschel/
Supervisory Patent Examiner, Art Unit 1614